Oncologic Emergencies for the Non-Oncologist

Jason Bischof, MD, FACEP
Assistant Professor
Department of Emergency Medicine
The Ohio State University Wexner Medical Center

Disclosures

• I have no financial conflicts to report related to this presentation.

• Other research support for unrelated projects:
  • Beckman Coulter
  • PCORI
  • The Ohio Attorney General’s Office
Objectives

1. Explain the state of acute oncology for the emergency medicine clinician.
2. Describe common acute complications experienced by oncology patients.
3. Discuss current deficits seen by emergency medicine clinicians in the acute care of oncology patients.
4. Describe the care coordination for oncology patients across medical specialties.
Current state of unscheduled acute care

Trends in Adult Cancer-Related Emergency Department Utilization: An Analysis of Data From the Nationwide Emergency Department Sample.

Abstract

IMPORTANCE: The emergency department (ED) is used to manage cancer-related complications among the 16.5 million people living with cancer in the United States. However, ED utilization patterns by the population of US adults with cancer have not been previously evaluated or described in published literature.

OBJECTIVE: To estimate the proportion of US ED visits made by adults with a cancer diagnosis, understand the clinical presentation of adult patients with cancer in the ED, and examine factors related to inpatient admission within this population.

DESIGN, SETTING, AND PARTICIPANTS: Nationally representative data comprised of 7 survey cycles (January 2006-December 2012) from the Nationwide Emergency Department Sample were analyzed. Identification of adult (age ≥18 years) cancer-related visits was based on Clinical Classifications Software diagnoses documented during the ED visit. Weighted frequencies and proportions of ED visits among adult patients with cancer by demographic, geographic, and clinical characteristics were calculated. Weighted multivariable logistic regression was used to examine the associations between inpatient admission and key demographic and clinical variables for adult cancer-related ED visits.

MAIN OUTCOMES AND MEASURES: Adult cancer-related ED utilization patterns. Identification of primary reason for ED visit; patient-related factors associated with inpatient admission from the ED.

RESULTS: Among an estimated 96.4 million weighted adult ED visits from January 2006 to December 2012, 29.5 million (31.2%) were made by a patient with a cancer diagnosis. The most common cancers associated with an ED visit were breast, prostate, and lung cancer, and most common primary reasons for visit were pneumonia (4.5%), nonspecific chest pain (3.7%), and urinary tract infection (2.3%). Adult cancer-related ED visits resulted in inpatient admissions more frequently (28.7%) than non-cancer-related visits (16.3%) (P < 0.001). Sepsis (odds ratio [OR], 91.2; 95% CI, 91.2-102.3) and intestinal obstruction (OR, 16.9; 95% CI, 16.5-17.4) were associated with the highest odds of inpatient admission.

CONCLUSIONS AND RELEVANCE: Consistent with national prevalence statistics among adults, breast, prostate, and lung cancer were the most common cancer diagnoses presenting to the ED. Pneumonia was the most common reason for adult cancer-related ED visits with an associated high inpatient admission rate. This analysis highlights cancer-specific ED clinical presentations and the opportunity to inform patient and system-directed prevention and management strategies.

Comprehensive Oncologic Emergencies Research Network (CONCERN)

Overview
Established in March 2015
Open scientific forum for oncology and emergency medicine researchers.
Goal: Accelerate knowledge generation, synthesis and translation of oncologic emergency medicine research through multi-center collaborations.

https://epi.grants.cancer.gov/concern/
### Table 2. Most Common ED Diagnoses Among 1075 Patients With Active Cancer

<table>
<thead>
<tr>
<th>ICD-10-CM Code</th>
<th>ICD-10-CM Category</th>
<th>Frequency, No. (%) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>R10</td>
<td>Abdominal and pelvic pain</td>
<td>100 (9.3) [7.6-11.2]</td>
</tr>
<tr>
<td>R50</td>
<td>Fever of other and unknown origin</td>
<td>87 (8.1) [6.5-9.9]</td>
</tr>
<tr>
<td>R06</td>
<td>Abnormalities of breathing</td>
<td>77 (7.2) [5.7-8.9]</td>
</tr>
<tr>
<td>R11</td>
<td>Nausea and vomiting</td>
<td>60 (5.6) [4.3-7.1]</td>
</tr>
<tr>
<td>R07</td>
<td>Pain in throat and chest</td>
<td>51 (4.7) [3.6-6.2]</td>
</tr>
<tr>
<td>D64</td>
<td>Other anemias</td>
<td>47 (4.4) [3.2-5.8]</td>
</tr>
<tr>
<td>E87</td>
<td>Other disorders of fluid, electrolytes, and acid-base balance</td>
<td>47 (4.4) [3.2-5.8]</td>
</tr>
<tr>
<td>R53</td>
<td>Malaise and fatigue</td>
<td>45 (4.2) [3.1-5.6]</td>
</tr>
<tr>
<td>E86</td>
<td>Volume depletion</td>
<td>43 (4.0) [2.9-5.4]</td>
</tr>
<tr>
<td>I26</td>
<td>Pulmonary embolism</td>
<td>39 (3.6) [2.6-4.9]</td>
</tr>
</tbody>
</table>

Abbreviations: ED, emergency department; ICD-10-CM, International Statistical Classification of Diseases, Tenth Revision, Clinical Modification.

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### Table 2. Most Common ED Diagnoses Among 1075 Patients With Active Cancer (Continued)

<table>
<thead>
<tr>
<th>ICD-10-CM Code</th>
<th>ICD-10-CM Category</th>
<th>Frequency, No. (%) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>J18</td>
<td>Pneumonia, unspecified organism</td>
<td>39 (3.6) [2.6-4.9]</td>
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<tr>
<td>D70</td>
<td>Neutropenia</td>
<td>37 (3.4) [2.4-4.7]</td>
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<tr>
<td>C34</td>
<td>Malignant neoplasm of bronchus and lung</td>
<td>36 (3.3) [2.4-4.6]</td>
</tr>
<tr>
<td>N39</td>
<td>Other disorders of urinary system</td>
<td>36 (3.3) [2.4-4.6]</td>
</tr>
<tr>
<td>R19</td>
<td>Other symptoms and signs involving the digestive system and abdomen</td>
<td>36 (3.3) [2.4-4.6]</td>
</tr>
<tr>
<td>C79</td>
<td>Secondary malignant neoplasm of other and unspecified sites</td>
<td>35 (3.3) [2.3-4.5]</td>
</tr>
<tr>
<td>M54</td>
<td>Dorsalgia (eg, radiculopathy, sciatica)</td>
<td>33 (3.1) [2.1-4.3]</td>
</tr>
<tr>
<td>G89</td>
<td>Pain, not elsewhere classified</td>
<td>28 (2.6) [1.7-3.7]</td>
</tr>
<tr>
<td>M79</td>
<td>Other and unspecified soft tissue disorders, not elsewhere classified (ie, nonspecific pain)</td>
<td>26 (2.4) [1.6-3.5]</td>
</tr>
<tr>
<td>R55</td>
<td>Syncope and collapse</td>
<td>26 (2.4) [1.6-3.5]</td>
</tr>
</tbody>
</table>

Abbreviations: ED, emergency department; ICD-10-CM, International Statistical Classification of Diseases, Tenth Revision, Clinical Modification.
What do the rest of us know?

ABFM In-Training Examination Content

<table>
<thead>
<tr>
<th>Topic</th>
<th>Content %</th>
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<th>Content %</th>
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<tbody>
<tr>
<td>Cardiovascular</td>
<td>12</td>
<td>Nonspecific</td>
<td>9</td>
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<tr>
<td>Endocrine</td>
<td>8</td>
<td>Psychogenic</td>
<td>7</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>7</td>
<td>Reproductive – Female</td>
<td>4</td>
</tr>
<tr>
<td>Hematologic/Immune</td>
<td>3</td>
<td>Reproductive – Male</td>
<td>1</td>
</tr>
<tr>
<td>Integumentary</td>
<td>6</td>
<td>Respiratory</td>
<td>13</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>12</td>
<td>Special Sensory</td>
<td>2</td>
</tr>
<tr>
<td>Nephrologic</td>
<td>3</td>
<td>Population-based Care</td>
<td>5</td>
</tr>
<tr>
<td>Neurologic</td>
<td>3</td>
<td>Patient-based Systems</td>
<td>5</td>
</tr>
</tbody>
</table>

The 2019 Model of the Clinical Practice of Emergency Medicine

The 2019 revision of the EM Model resulted in significant changes and clarifications, including the addition of an oncology section within Category 8, Hematologic and Oncologic Disorders

- Febrile Neutropenia
- Hypercalcemia of Malignancy
- Hyperviscosity Syndrome
- Malignant Pericardial Effusion
- Spinal Cord Compression
- Superior Vena Cava Syndrome
- Tumor Hemorrhage
- Tumor Lysis Syndrome


EM Education – How are we doing?

Rajha et al. surveyed EM program directions (The American Journal of Emergency Medicine, 2020)

- Oncology topics are critical in the preparation of EM trained physicians?
  
  Disagree: 4%
  Neither Agree or Disagree: 6%
  Agree: 75%
  Strongly Agree: 16%

- Our EM residency program's didactic curriculum fully prepares residents for the recognition and management of oncologic emergencies.
  
  Disagree: 14%
  Neither Agree or Disagree: 22%
  Agree: 59%
  Strongly Agree: 6%
Febrile Neutropenia

- Single oral temperature measurement of $\geq 38.3^\circ C$ (101°F) or a temperature of $\geq 38.0^\circ C$ (100.4°F) sustained over a 1 hour period
  - And
- Severe neutropenia that is defined as an absolute neutrophil count (ANC) of $<500$ cells/mm$^3$ or expected during the next 48 hours
- Multiple etiologies including myelosuppression secondary to chemotherapy

https://www.mdcalc.com/masc-risk-index-febrile-neutropenia#evidence
Hypercalcemia

- Presentation:
  - GI symptoms, Neurologic changes, renal failure

- Severity:
  - Degree and rate of onset

- Causes:
  - Humoral: parathyroid hormone-related protein (PTHrP) secretion (80%)
  - Osteolytic (20%)
  - Vitamin D secretion
  - Ectopic PTH

- Treatment: Fluids, bisphosphonates, calcitonin, monoclonal antibody (Denosumab), avoid loop diuretics (volume dependent)

Hyperviscosity Syndrome

- Pathological increase in serum proteins, red blood cells (RBC), white blood cells (WBC), or platelets
- Triad: Neurologic deficits, bleeding, and visual changes (low flow state and platelet dysfunction)
- Waldenstrom Magroglobulinemia (10-30%), Myeloma (3-6%)
- Treatment: Plasmapheresis, Avoid dehydration (1-2L fluids), Treat etiology (Chemotherapy)

Malignant Pericardial Effusion

- Most often caused by lung cancer, breast cancer, melanoma, lymphoma, and leukemia.
- Chemotherapeutic agents (e.g., cyclophosphamide, cytarabine, dasatinib, doxorubicin, gemcitabine).
- Beck’s triad (hypotension, jugular venous distention, and muffled heart sounds) less likely due to slow accumulation.
- Intervention dependent of clinical stability.

Author: Jer5150 (CC BY-SA 3.0)

Weaver et al. Front Oncol. 2020 May 19;10:815

Malignant Spinal Cord Compression

- Etiology: Primary invasion, Metastatic lesions, Pathologic fracture
- Back pain, focal neurologic deficits
- Associated with breast, lung, prostate, and kidney cancer, lymphoma and multiple myeloma
- Acute neurologic findings requires urgent MRI evaluation
- Multiple grading systems, symptom (Frankel) and imaging based (ESCC)
- Treatment: Dexamethasone 10-16mg IV, Chemotherapy/Radiation/Surgery depending on tumor type

Ropper AE, Ropper AH. N Engl J Med ;376:1358-1369
https://www.nice.org.uk/guidance/cg75/chapter/1-Guidance#the-patients-experience-of-mscc

Superior Vena Cava (SVC) Syndrome

- Blockage of thin walled SVC
  - Generally malignancy: Lung Cancer, Non-Hodgkin’s Lymphoma
  - Other causes: Catheter associated thrombosis, infection, thymoma, autoimmune disorders
- Swelling of the face, neck, arms, neck (edema including pleural and cerebral)
- Grading based on symptoms/involvement of azygous vein.
- Treatment dependent on etiology: Head of bed elevated, Airway management, Steroids, Chemotherapy, Radiation therapy, Stenting, bypass, Thrombolysis

Tumor Hemorrhage

- Management dependent on location and severity
- Due to malignancy or treatment adverse effects
- Assess for anticoagulation and reverse as appropriate
- Co-management with appropriate consulting service

- In a sample of 555 patients on Immune Checkpoint Inhibitors: Clinically significant bleeding and thrombocytopenia at 3 months of treatment were identified in 21% and 7%.

Tumor Lysis Syndrome

- Tends to occur in rapidly dividing tumors.
- Rapid release of potassium, phosphorous, nucleic acids, and cytokines.
- Laboratory definition: ≥2 abnormal serum values or a 25% change in value of uric acid, potassium, phosphorous, and calcium.

- Treatment: fluids, allopurinol, rasburicase, serial electrolyte monitoring, dialysis
  - no role for urine alkalinization
Current Deficits

Gaps in Current Curriculum
- Immunotherapy Treatments and Associated Side Effects
- Symptom and side effect management in Cancer Patients
- Surgical Procedures and Complications in Patients with Cancer
- Effects of Oncology Treatment on Common Emergency Presentations
- Need for Emergent Oncological Treatment for the Newly Diagnosed Cancer Patient with Cancer

Gaps in Research Efforts
- Care Utilization Across the Age Continuum and Rural/Urban Divide
- Risk Stratification
- Diagnostic Pathways
- Implementation Science Barriers to Oncology Evidence-Based Medicine
- Social Determinant of Health Affecting Acute Presentation

Immunotherapy ≠ Chemotherapy
**Other Major Classes of Immunotherapy:**
- Oncologic Vaccines
- Cytokines
- Viral Therapy

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Proportion of US patients with cancer were eligible for immune checkpoint inhibitor therapy
1.5% (2011) --> 36% (2019)

Immune Related Adverse Events (irAEs)

- All organ systems are potentially affected.
- Presentation is often delayed weeks, months and even years later.

- Eyes: Uveitis, Conjunctivitis
- Endocrine: Hypo/hyperthyroidism, hypopituitarism, hypophysitis, adrenal insufficiency
- Cardiovascular: Myocarditis, Pericarditis, Vasculitis
- Gastrointestinal: Colitis
- Musculoskeletal: Arthritis, Dermatomyositis
- Neurologic: Neuropathy, Myelopathy, Encephalitis, Myasthenia
- Respiratory: Pneumonitis, Pleuritis
- Liver: Hepatitis
- Renal: Nephritis
- Dermatologic: Rash, Vitiligo, Rash

Common Terminology for Adverse Events (CTCAE)

Introduction
The NCI Common Terminology Criteria for Adverse Events is a descriptive terminology which can be utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term.

SOC
System Organ Class (SOC), the highest level of the MedDRA
1
 hierarchy, is identified by anatomical or physiological system, etiology, or purpose (e.g., SOC investigations for laboratory test results). CTCAE terms are grouped by MedDRA Primary SOC. Within each SOC, AEs are listed and accompanied by descriptions of severity (scale).

CTCAE Terms
An Adverse Event (AE) is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure. An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses. Each CTCAE v4.0 term is a MedDRA LIL (lowest level term).

Grades
Grade refers to the severity of the AE. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

Grade 1 Mild: asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2 Moderate: minimal, local or conservative intervention indicated; limiting activities of daily living (ADLs) or work or leisure activities.
Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADLs.
Grade 4 Life-threatening consequences; urgent intervention indicated.
Grade 5 Death related to AE.

A semi-colon indicates ‘or within the description of the grade.

A single dash (-) indicates a Grade is not available.

Not all Grades are appropriate for all AEs. Therefore, some AEs are listed with fewer than five options for Grade selection.

Definitions
A brief Definition is provided to clarify the meaning of each AE term. A single dash (-) indicates a Definition is not available.

Navigational Notes
A Navigational Note is used to assist the reporter in choosing a correct AE. It may list other AEs that should be considered in addition to, or in place of, the AE in question. A single dash (-) indicates a Navigational Note has not been defined for the AE term.

Activities of Daily Living (ADLs)
Instrumental ADLs refer to preparing meals, shopping for groceries, or clothes, using the telephone, managing money, etc.

Self-care ADLs refer to bathing, dressing, and undressing, feeding self, using the toilet, taking medications, and bowel/bladder management.

https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf
**Cytokine Release Syndrome (CRS)**

- Presents from mild to severe symptoms
  - fatigue $\rightarrow$ hypotensive shock and respiratory failure.

- Treatment: Supportive care as necessary

- Grading based on need for supportive measures

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**Immune Effector Cell-Associated Neurotoxicity syndrome (ICANS)**

- Symptoms range from non specific neurologic symptoms (Fatigue) to Seizures, Coma and Death 2/2 cerebral edema

- Graded by alterations to mental status

- Onset typically 3-10 days after treatment

- Evaluation: Altered Mental Status evaluation + LP + MRI

- Treatment: Supportive care seizure prophylaxis $\pm$ tocilizumab $\pm$ steroids

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https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.html
Care Coordination – Wrap Around Care

- irAE diagnosis is a diagnosis of exclusion dependent on obtaining an accurate history (integration of medical record)
- Clear communication/coordination with the primary oncologist
- Immunotherapy Wallet Cards
- Emergency Physician is part of the Oncology Team
- Need for adoption/endorsement of Oncology Guidelines by Non-Oncology Organizations

Joint Models of Acute Care

- Nurse Navigation extending from the Oncology Clinic/Ward to the ED
  - When surveyed, 91% of participants at an oncology navigation conference reported that navigation services in the ED would be either moderately or very helpful.

- Hybrid Care Sites
  - Nurse Triage Line for acute care in Cancer Hospital Infusion Center versus Emergency Department
  - The James Immediate Care Center
  - Integrated Oncology Pods
  - Clear Referral Patterns – Diagnostic Center
Emergencies unrelated to the primary oncologic diagnosis,..., may occur. For this reason routine emergency protocols and diagnostic procedures should be followed in the treatment of oncology patients.”